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Proposed Re-evaluation Decision

Oxirane Derivatives

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Overview

What is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial oxirane derivatives, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing oxirane derivatives in Canada.

An evaluation of available scientific information found that products containing oxirane derivatives do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of oxirane derivatives uses, new risk-reduction measures must be included on the labels of all products. No additional data are being requested at this time.

This proposal affects all end-use products containing oxirane derivatives registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for oxirane derivatives and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of oxirane derivatives.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks as well as value of pesticide products, to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Oxirane derivatives, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2005 RED, the USEPA concluded that oxirane derivatives were eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What are Oxirane Derivatives?

Oxirane derivatives are an equilibrium mixture of three components. This antimicrobial is used as a material preservative in adhesives, caulks and sealants, latex emulsion, ink, latex paint, pigment dispersion and slurry, and paper coatings and printing colours. It is handled by professional workers during introduction of the active ingredient as a materials preservative through liquid pour or pump application during manufacture of the material. Homeowners can use household products which already contain this active ingredient.

Health Considerations

Can Approved Uses of Oxirane Derivatives Affect Human Health?

Oxirane derivatives are unlikely to affect your health when used according to the revised label directions.

People could be exposed to oxirane derivatives while working with treated materials during their manufacture or through residential exposure (i.e. homeowners may be exposed during application of the treated product, or postapplication to the treated materials (e.g. paint). The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that oxirane derivatives are unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Environmental Considerations

What Happens When Oxirane Derivatives are Introduced Into the Environment?

Oxirane derivatives are unlikely to affect non-target organisms when used according to the revised label directions.

Based on a qualitative risk assessment, the USEPA determined that indoor uses of oxirane derivatives were not likely to result in unacceptable ecological risk to non-target organisms based on minimal exposure potential and low to slight toxicity.

The USEPA concluded that oxirane derivatives were unlikely to affect non-target organisms provided that risk reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation and equivalent risk reduction measures are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of oxirane derivatives, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Updated protective equipment statement to protect workers
- Addition of signal words "potential skin sensitizer" to protect workers
- Reduction in concentration added to paint (maximum 0.20% by weight) to protect homeowners

Environment

- Additional advisory label statements to reduce potential surface and groundwater contamination

Next Steps

Before making a final re-evaluation decision on oxirane derivatives, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Oxirane derivatives are an antimicrobial pesticide, which acts as a material preservative for the control of bacteria in adhesives, caulks and sealants, latex emulsion, ink, latex paint, pigment dispersion and slurry, and paper coatings and printing colours.

Following the re-evaluation announcement for oxirane derivatives, the registrant of the technical grade active ingredient in Canada indicated they would continue to support all uses included on the labels of commercial end-use products in Canada.

The PMRA used recent assessments of oxirane derivatives from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for azadioxabicyclooctane (i.e. oxirane derivatives), dated September 2005, as well as other information on the regulatory status of azadioxabicyclooctane in the United States, can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

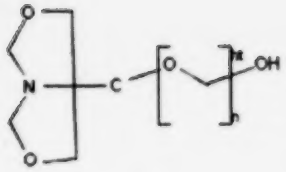
2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

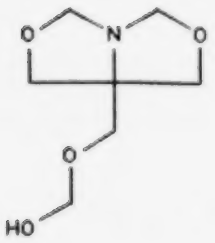
Common name	Oxirane derivatives (equilibrium mixture of three acetyls) (referred to as "azadioxabicyclooctane" in the US)
Function	Material preservative, microbiocide
Chemical class	Bicyclic oxazolidine
Chemical name	
1 **International Union of Pure and Applied Chemistry (IUPAC)**	5-hydroxymethoxymethyl-1-aza-3,7-dioxabicyclo(3,3,0)octane; 5-hydroxymethyl-1-aza-3,7-dioxabicyclo(3,3,0)octane; 5-hydroxypoly(methylene-oxy)methyl-1-aza-3,7-dioxabicyclo(3.3.0)octane (74%C2, 21%C3, 4%C4,1% C5)
2 **Chemical Abstract Service Registry Number (CAS)**	107497-96-1 (for the mixture)
Molecular formula	$C_7H_{13}O_4N$ (for 59720-42-2)

Structural formula

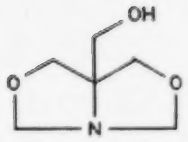
56709-13-8



59720-42-2



6542-37-6



Molecular weight	171 (for 59720-42-2)
Purity of the technical grade active ingredient	50% minimum concentration unconfirmed
Registration Number	27359

In 1985 nitrosamine analyzes were performed on 2 batches of Reg. No. 27359 and none were detected at an limit of detection (LOD) of 1 parts per million (ppm).

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4, or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20°C	Components A and B: 4 - 30 × 10^{-4} mm Hg Component C: Likely to have less volatility
Solubility in water at 25°C	Soluble in all proportions
n-octanol–water partition coefficient at 22°C	log K_{ow} = -1.11
Dissociation constant	not applicable

2.3 Comparison of Use Patterns in Canada and the United States

Oxirane derivatives are an antimicrobial pesticide registered in Canada used to prevent bacterial spoilage in water-based products. It is used as a preservative in adhesives, latex based caulks and sealants, latex emulsions, ink, latex paints, pigment dispersions and slurries, and paper coatings and printing colours. The only registered commercial end-use product is formulated as a solution with a guarantee of 50% and is for industrial use only. The maximum registered concentration in treated materials is 0.25% oxirane derivatives. Although there are no registered domestic (i.e. homeowner) oxirane derivatives products registered in Canada or in the US, there is a potential for residential exposure from the use of oxirane derivatives-treated paint by homeowners (i.e. via airless spraying and brush painting).

The American and Canadian use patterns were compared. The Canadian formulation type of the end-use product and the uses of oxirane derivatives as a material preservative are among those registered in the United States. The Canadian maximum allowable concentration of 0.25% of material treated is encompassed by that registered in the United States (0.25% active ingredient of material treated). Based on this comparison of use patterns, it was concluded that the USEPA RED for azadioxabicyclooctane is an adequate basis for the re-evaluation of the Canadian uses of oxirane derivatives.

All current uses are being supported by the registrant and were considered in the re-evaluation of oxirane derivatives. Appendix I lists all oxirane derivatives products registered as of 13 August 2007 under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In the 2005 RED, the USEPA concluded that the end-use products formulated with oxirane derivatives met the safety standard under the American *Food Quality Protection Act* (FQPA) and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to the effects of a chemical than the most sensitive animal species.

Exposure to oxirane derivatives may occur while working with treated materials during their manufacture, through postapplication exposure to treated materials or through residential exposure (i.e. homeowners may be exposed during application of the treated product, or postapplication to the treated materials such as paint). In the United States, exposure may also occur through consumption of food as a result of its use as a preservative in paper coating and paper adhesives.

When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required. The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix II.

Workers can be exposed to oxirane derivatives through handling the pesticide or through postapplication exposure to treated materials.

3.1.1.1 Handler Exposure and Risk

Nine potential occupational inhalation/dermal exposure scenarios for workers were identified. Among the exposure scenarios assessed in the RED, the following were considered to be relevant to the Canadian situation:

- introduction of active ingredient (a.i.) as a materials preservative into latex paint (liquid pour)
- introduction of a.i. as a materials preservative into latex paint (liquid pump)
- introduction of a.i. as a materials preservative into paper coating (liquid pump)
- professional painter applying "already preserved" paint by brush/roller
- professional painter applying "already preserved" paint by airless sprayer

Latex paints are representative for exposure to adhesives, caulks, ink dispersions, pigment dispersions, pigment slurries and sealants. Handler exposure analyses were performed using surrogate data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 and an antimicrobial study conducted by the Chemical Manufacturers' Association (CMA), assuming workers were wearing a long-sleeved shirt, long pants and chemical-resistant gloves. Short-term and intermediate dermal and inhalation risk were based on a maximum oxirane derivatives concentration of 0.25% a.i. by weight of material being treated, using a dermal target margin of exposure (MOE) of 300 (including a threefold uncertainty factor for lack of a no-observed adverse effects level (NOAEL) based on a lowest observed adverse effects level (LOAEL) of 100 mg/kg bw/day in a 21-day dermal toxicity study in rabbits), and an inhalation target MOE of 300 (including a threefold uncertainty factor for lack of histopathological data) based on a NOAEL of 10.6 mg/kg bw/day in a 90-day oral toxicity study in rats.

The USEPA reported acceptable short-term and intermediate-term dermal and inhalation MOEs for the above occupational exposure scenarios, ranging from 400 to 120 000 (MOE >300). Based on this quantitative assessment, no mitigation measures were required.

The RED adequately addressed potential occupational exposure scenarios associated with the uses of products containing oxirane derivatives in Canada and conclusions derived from the RED apply to the Canadian situation. Based on this, the PMRA requires that the signal words "POTENTIAL SKIN SENSITIZER" be added to the label. In addition, the Canadian label currently requires that workers (i.e. for industrial use) wear goggles or face shield, protective clothing, rubber gloves and a respirator when handling the product. While this is considered adequate, to be consistent with current label terminology, the PMRA requires that the registrant amend the statement such that industrial handlers wear goggles or face shield, long pants, a long-sleeved shirt, shoes plus socks, chemical-resistant gloves and a respirator during mixing, loading, clean-up and repair. The proposed label amendments are listed in Appendix III.

3.1.1.2 Postapplication Exposure and Risk

It was determined that potential occupational postapplication exposures could result from bystanders coming into contact with areas in which the active had recently been applied. The USEPA expected exposures to be minimal for scenarios relevant to the Canadian use pattern.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of oxirane derivatives and conclusions derived from the RED apply to the Canadian situation. Based on this, no mitigation measures are required.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach as explained for the occupational exposure and risk assessment in Section 3.1.1 above. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix II.

Homeowners can be exposed to oxirane derivatives through handling paints, caulks, sealants or ink containing oxirane derivatives. Potential dermal and inhalation exposure and risk to adults from applying treated paint or postapplication exposure to adults exposed to recently applied treated paint were assessed (i.e. paint was considered the highest exposure scenario). Based on end-use product application methods and use amounts, it was assumed that exposures while applying paints would be equal to or greater than exposures that may occur when an individual uses any of the other end use products (i.e. caulks, inks and sealants). The duration of exposure was considered to be short-term. Handler exposure analyses were performed using surrogate data from PHED, version 1.1, based on application of two gallons of treated paint with a brush or roller in one day, and application of 15 gallons of treated paint with an airless sprayer in one day, with treated paint containing 0.25% a.i. The dermal target MOE was 300 (including a threefold uncertainty factor for lack of a NOAEL) based on a LOAEL of 100 mg/kg bw/day in a 21-day dermal toxicity study in rabbits), and the inhalation target MOE was 3000 (including an FQPA factor of 10-fold based on developmental (dermal only) and reproductive toxicity databases, and a threefold uncertainty factor due to a lack of histopathology data) based on a NOAEL of 10.6 mg/kg bw/day in a 90-day oral toxicity study in rats. Acceptable adult handler short-term dermal MOEs ranging from 609 to 1181 (>300) and inhalation MOEs ranging from 12 000 to 53 000 (>3000) were reported for most scenarios. However, short-term exposures of concern were identified for both dermal (MOE = 236) and inhalation (MOE = 2400) exposures for handlers using an airless sprayer to apply oxirane derivatives-treated paint containing 0.25% a.i. It was determined that risk was acceptable when 0.2% a.i.-treated paint was applied using an airless sprayer. Therefore, the maximum concentration of oxirane derivatives in paint must be reduced from 0.25% to 0.20% a.i. by weight of material treated.

The USEPA concluded that postapplication exposure to bystanders coming into contact with areas in which the treated material (i.e. paint) had been recently applied was expected to be minimal due to the paint being dry (expected to dry within a day) and to the negligible vapour pressure of oxirane derivatives. The USEPA did not identify potential postapplication exposures to children.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of oxirane derivatives (i.e. paint, caulks and sealants) in Canada; thus, the conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires that the registrant reduce the maximum allowed concentration in paint from 0.25% a.i. by weight to 0.2% a.i. by weight of paint treated.

3.1.2.2 Exposure From Food and Drinking Water

In the United States, oxirane derivatives could have indirect contact with food as a result of its use as a preservative in paper coating and paper adhesives. It was reported to have been approved by the United States Food and Drug Administration (USFDA) for use as an antibacterial preservative in paper and paperboard products having contact with dry food only and as a component in paper adhesives.

Tier I acute and chronic dietary (food) exposure and risk assessments were conducted, resulting in exposure of 12% of the acute population adjusted dose (aPAD) and 39.6% of the chronic population adjusted dose (cPAD) for children one to six years old, the most sensitive subpopulation. The acute risk assessment was based on an aPAD of 0.01 mg a.i./kg bw/day, which was calculated from a 90-day oral toxicity study in rats (NOAEL of 10.6 mg/kg bw/day and an FQPA factor of 10 fold). The chronic risk assessment was based on a cPAD of 0.003 mg a.i./kg bw/day, which was calculated from the same study, which included an additional threefold uncertainty factor for lack of a chronic study. Assumptions in both risk assessments were "worst-case" dietary concentration values, based on a maximum concentration of 0.25% a.i. by weight of the paper coating, USFDA's default assumptions for preservation of paper adhesives, and the USEPA's standard body weights. The USEPA considered the estimated acute and chronic exposures from food to be below its levels of concern and no mitigation with respect to dietary risk was required.

The USEPA determined that none of the uses associated with oxirane derivatives were expected to have an impact on either surface or groundwater resources. In addition, modelling data indicated that rapid biodegradation was highly probable in soils and water. Therefore, no drinking water assessment was performed.

In Canada, the acceptability of the use of material preservatives that can come into contact with food is assessed by the Bureau of Chemical Safety, Food Directorate of Health Canada. The Bureau of Chemical Safety has not issued an opinion indicating that it has no objection to the use of Nuosept 95 in paper or paperboard that may contact food. Based on this, the PMRA requires that the statement "Not for use in the production of paper or paperboard that will come into contact with food." must be added to the Nuosept 95 end-use product label in Canada. The Bureau of Chemical Safety did issue an opinion indicating that it has no objection to the use

of Nuosept 95 as a preservative at a maximum level of 0.2% in coatings (paints) which are applied to equipment and structural surfaces of Federally Registered Meat Establishments. The food contact from this use is expected to be negligible and therefore a label statement for this use is not required.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to oxirane derivatives (i.e. from food, water and residential exposures).

Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures.

Short-term and intermediate aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal and inhalation).

For oxirane derivatives, acute and chronic aggregate risks were based on indirect food exposures only. As discussed above, these risks were considered acceptable. Short-term aggregate risk for adult handlers combined dietary exposure and residential inhalation and dermal exposure, and was of concern for the scenario of paint containing 0.25% a.i. oxirane derivatives applied via airless sprayer. As discussed above, the USEPA required that the registrant reduce the maximum allowable concentration in treated paint from 0.25% a.i. to 0.2% a.i. by weight.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of oxirane derivatives in Canada and equivalent risk reduction measures are required.

3.1.3 Cumulative Effects

The USEPA has not determined whether oxirane derivatives has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that oxirane derivatives does not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

The USEPA determined that none of the uses associated with oxirane derivatives were expected to have an impact on either surface or groundwater resources. In addition, modelling data indicated that quick biodegradation was highly probable in soils and water. With a log *n*-octanol–water partition co-efficient (K_{ow}) of -1.11, it was concluded that oxirane derivatives were not likely to bioaccumulate in aquatic organisms.

The USEPA did not conduct any quantitative ecological risk assessments. They determined that, based on the use pattern, most of the uses of oxirane derivatives were indoors. The USEPA concluded that indoor uses of oxirane derivatives were not likely to result in unacceptable ecological risk to non-target organisms based on minimal exposure potential and low to slight toxicity. No mitigation measures were required.

The United States use pattern for oxirane derivatives encompasses the Canadian use pattern. Based on the RED and in consideration of the Canadian situation, the PMRA requires an additional advisory label statement. Appendix III lists all label amendments.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy, a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of oxirane derivatives. The PMRA has reached the following conclusions.

- Oxirane derivatives were not found to be persistent and are not bioaccumulative; the *n*-octanol–water partition coefficient (log K_{ow}) is -1.11, which is below the TSMP Track 1 cut-off criterion of 5.0. Oxirane derivatives do not meet all Track 1 criteria and thus are not a candidate for Track 1 classification.

- In 1985 nitrosamine analyses were performed on two batches of the product having Registration Number 27359 and none were detected at an LOD of 1 ppm. Based on a review of the available chemistry information (see Section 2.1), the oxirane derivatives technical product is not expected to contain any other impurities of toxicological concern as identified in Section 2.13.4 of Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Appendix II of Regulatory Directive DIR99-03.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 Proposed Re-evaluation Decision

The PMRA has determined that oxirane derivatives is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. No additional data are being requested at this time.

5.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

Information regarding food packaging materials is available through Health Canada's website at www.hc-sc.gc.ca/fn-an/securit/packag-emball/index_e.html

The USEPA RED document for azadioxabicyclooctane is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

°C	Celsius
a.i.	active ingredient
aPAD	acute population adjusted dose
bw	body weight
CAS	Chemical Abstracts Service
CMA	Chemical Manufacturers' Association
aPAD	acute population adjusted dose
cPAD	chronic population adjusted dose
DACO	data code
FQPA	*Food Quality Protection Act*
g	gram(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LOAEL	lowest observed adverse effect level
LOD	limit of detection
m	metre(s)
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
NOAEL	no observed adverse effect level
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RED	Reregistration Eligibility Decision
RVD	Re-evaluation Decision
SF	Safety factor
TSMP	Toxic Substances Management Policy
UF	Uncertainty factor
US	United States
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration

Appendix I Registered Products Containing Oxirane Derivatives as of 13 August 2007

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
27359	Technical	ISP Canada Inc.	Nuosept 95 Technical	Solution	50
19201	Commercial	ISP Canada Inc.	Nuosept 95 Preservative	Solution	50

Appendix II Toxicological Endpoints for Oxirane Derivatives Health Risk Assessments

Exposure Scenario (route and period of exposure)	Dose (mg/kg bw/day)	Study	Target UF/SF or MOE[a]
Dietary acute	Oral NOAEL = 10.6	90-day oral toxicity study in rats	UF = 100 FQPA SF = 10 fold **aPAD = 0.01 mg/kg bw/day**
Dietary chronic	Oral NOAEL = 10.6	90-day oral toxicity study in rats	UF = 300 FQPA SF = 10 fold **cPAD = 0.003 mg/kg bw/day**
Dermal (occupational short- and intermediate-term)	Dermal LOAEL = 100	21-day dermal toxicity study in rabbits	UF = 300 (including 3 fold for lack of NOAEL) **target MOE = 300**
Dermal (residential, short-term and intermediate	Dermal LOAEL = 100	21-day dermal toxicity study in rabbits	UF = 300 (including 3 fold for lack of NOAEL) **target MOE = 300**
Inhalation (occupational) (all durations)	Oral NOAEL = 10.6	90-day oral toxicity study in rats	UF = 300 (including 3 fold for database uncertainty) **target MOE = 300**
Inhalation (residential)	Oral NOAEL = 10.6	90-day oral toxicity study in rats	UF = 3000 (including 3 fold for database uncertainty and 10 fold FQPA safety factor which was retained based on the lack of developmental and reproductive toxicity data) **target MOE = 3000**

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments. MOE refers to desired margin of exposure for occupational or residential assessments.

Appendix III Label Amendments for Products Containing Oxirane Derivatives

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The PMRA requires that the label be modified so that oxirane derivatives is added to paint at a maximum concentration of 0.2% a.i. by weight (i.e. 0.4% product by weight).

II) The following statement must be removed from the section entitled **DIRECTIONS FOR USE.**

> **Food Contact Application**: NUOSEPT 95 Preservative cannot be used in direct or indirect food contact applications unless the Bureau of Chemical Safety of Health Canada has issued an opinion indicating that it has no objection to the use of NUOSEPT 95 Preservative in such applications.

And the following statement must be included in the section entitled **DIRECTIONS FOR USE**.

> **NOT** for use in the production of paper or paperboard that will come into contact with food.

III) The following statements must be included in a section entitled **PRECAUTIONS**.

> Wear goggles or face shield, long pants, long-sleeved shirt, shoes plus socks, chemical-resistant gloves and a respirator during mixing, loading, clean-up and repair.
>
> POTENTIAL DERMAL SENSITIZER

IV) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

> DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

The PMRA will be undertaking initiatives to address the labelling deficiencies for certain kinds of antimicrobial products, especially with respect to the "Directions for Use" section of product labels. The PMRA will announce in the near future the nature of these initiatives and any requirements to be addressed by registrants.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.